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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/677,857	10/03/2003	Eugene R. Cooper	029318-0981	4616
31049 7590 09/15/2008 Elan Drug Delivery, Inc. c/o Foley & Lardner 3000 K Street, N.W. Suite 500 Washington, DC 20007-5109				
EXAMINER				
UNDERDAHL, THANE E				
ART UNIT		PAPER NUMBER		
1651				
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09/15/2008		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

**Advisory Action
Before the Filing of an Appeal Brief**

Application No.

10/677,857

Applicant(s)

COOPER ET AL.

Examiner

THANE UNDERDAHL

Art Unit

1651

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 07 April 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ They raise the issue of new matter (see NOTE below);
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
The status of the claim(s) is (or will be) as follows:
Claim(s) allowed: _____.
Claim(s) objected to: _____.
Claim(s) rejected: 1-10, 13-17, 56 and 57.
Claim(s) withdrawn from consideration: 11, 12 and 18-55.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____.
13. ☐ Other: _____.

/Irene Marx/
Primary Examiner, Art Unit 1651

1-10, 13-17, 56 and 57 remain obvious over Ramirez et al. The Examiner argued that even while Ramirez et al. teaches all limitations of claim 1 except that the size of the benzoyl peroxide (BP) particles is "less than about 2000nm". The Examiner addressed this deficiency in Ramirez et al. by stating that the size of the BP particles is a result effective variable and is recognized as such by Ramirez et al. since they teach "It would be desirable to provide a BP compositions...which have a smooth texture appropriate for cosmetic products" (col 1, lines 53-59) and Ramirez et al. teach a desire to "prepare a paste having benzoyl peroxide crystals that are sufficiently fine to be of acceptable texture for preparing products for topical use" (col 1, lines 30-40) (see Final Office Action, page 7, 2nd paragraph). The Examiner requested some evidence of criticality that shows a smaller particle size would achieve an unexpected result from Ramirez et al. to overcome this rejection.

The Applicant argued by stating "The particle size of benzoyl peroxide is critical, because the nanoparticulate compositions of benzoyl peroxide possess a number of advantages over the conventional microparticles of benzoyl peroxide." (Applicant's Response Page 17, last paragraph). The Applicant states the size of the BP particles is critical because small BP particles "may offer one or more of the following advantages: (1) faster onset of action; (2) a potential decrease in the frequency of dosing; (3) smaller doses of benzoyl peroxide required to obtain the same pharmacological effect; (4) improved performance characteristics, such as higher dose loading; (5) bioadhesive benzoyl peroxide formulations, which can coat the desired site of application and be retained for a period of time, thereby increasing the efficacy of the drug as well as eliminating or decreasing the frequency of dosing; (6) low viscosity liquid nanoparticulate benzoyl peroxide compositions, useful for topical application of liquid washes; (7) the nanoparticulate benzoyl peroxide compositions can be formulated in a dried form which readily redisperses, such as for reconstitution in a liquid to be used in a wash; (8) the nanoparticulate benzoyl peroxide compositions can be used in conjunction with other active agents; and (9) the nanoparticulate benzoyl peroxide compositions do not require organic solvents or pH extremes" (Applicant's response, page 19, lines 1-12). The Applicant cites the support for these advantages in paragraph [0026] of their specification. However neither this paragraph in the specification or in the examples provided show that these advantages are achieved or provide a comparison to the BP particles in the art. Simply stating advantages that the BP particle size "may offer" is not persuasive evidence of unexpected results over the prior art.

The Applicant argues that "not every combination of surface stabilizer and active agents will result in a stable nanoparticulate composition" (Applicant's Response, page 18, last paragraph) and cites paragraph [0024] in the specification as support for this statement. However paragraph [0024] in its entirety reads

"As taught in the '684 [US 5145684] patent, not every combination of surface stabilizer and active agent will result in a stable nanoparticulate composition. It was surprisingly discovered that stable nanoparticulate benzoyl peroxide formulations can be made." (Patent number Added by Examiner).

However '684 never mentions BP or provides teaches that "not every combination of surface stabilizer and active agent will result in a stable nanoparticulate composition". Indeed '684 teach a wide range of surface stabilizers with a variety of structures from gelatin, polyethylene glycols, colloidal silicon, phosphates and derivatized cellulose. The Examiner could not find a nexus in '684 between the specific structures of the stability of the particle and certainly could not find any teachings related to BP. Therefore the Applicant has not provided convincing evidence of unexpected results that overcome that the teachings of Ramirez et al. could not meet the limitations of claim 1 via routine optimization.

The Applicant continues to argue that the alkylbenzoate used by Ramirez et al. does not qualify as a surface stabilizer and is simply a solvent used to solubilize the BP particles (Applicant's Response page 19, paragraph 2).

However there is no limitation in the claims that the surface stabilizer cannot also be the solvent. Furthermore the Applicant defines a surface active stabilizer as preventing the BP particles from "appreciably flocculate or agglomerate due to interparticle attractive forces, or otherwise significantly increase in particle size over time" and that the structure of the BP particles "is not altered over time" and are "chemically stable".

However, Ramirez et al. meets these requirements since they teach when the alkylbenzoate is removed from the composition that a "fine amorphous powder" is obtained (col 3, lines 27-37). They also teach that the BP when mixed in a composition with alkylbenzoate "remains without intact, without any chemical changes" (col 3, lines 45-48). Ramirez et al. also teach that their composition has the consistency of a paste (col 3, lines 27-30) and does not indicate the BP particles appreciably flocculate or agglomerate to increase in particle size.

The Applicant argues that Ramirez does not teach surface stabilizers in claims 8, 10 and 12. However claim 12 is withdrawn as being drawn to a non-elected species which was acknowledged by the Applicant (Applicant's Response, page 16, II Species Election). Claim 8 is to a nonionic surface stabilizer and claim 10 lists colloidal silicon dioxide as one of the surface stabilizers limited in this composition. However the Examiner explicitly stated that Ramirez et al. taught the addition of colloidal silicon dioxide in the both office actions (See page 7 of Final Office action and page 3 of Non-Final Office action). Therefore these claim limitations are met.

The Applicant argues that Tarasov, Self and Bagchi et al. do not show that one of ordinary skill in the art at the time the invention was made would be able to make nanoparticulate BP. However the Applicant directly ignores the teachings of Bagchi et al. who teach such small particles of less than 400 nm (see Abstract). The Applicant directly ignored that the abstract of Bagchi et al. requires that surface active agents must be added to successfully precipitate particles of such small size (see Abstract). The Applicant also directly ignores that the surface active agents cited by the Examiner in Bagchi et al. are in some instances the same as those claimed by the Applicant (Final Office Action, page 3 last line, in particular see Bagchi col 3, lines 15-45 which cite "colloidal silicon dioxide", "polyethylene glycols"). The Applicant ignores the similarities of Tarasov and Bagchi et al. that provide the evidence that one of ordinary skill in the art would be able to make and optimize the size of BP particles before the invention was made. Furthermore the argument that Bagchi et al. simply teach "a laundry list of genera chemical compositions" and then cites columns 5 and 6 confuses the Examiner since there was no citation or reference to this section in the previous Office Action.

Applicants arguments based on KSR are noted, however they are not persuasive of error in the rejection, since the particles of the invention and the particles disclosed by the prior art are substantially similar and any modification would have been within the ordinary skill of the artisan in this art.

Applicants rely on the arguments used in traversing the above rejection of Ramirez et al. to also traverse the rejections of Ramirez et al. combined with Kanios and Bartrick without additional arguments. However, as explained above, the previous rejection stands. Therefore, the response set forth above to arguments also applies to this rejection. Therefore, the claims remain obvious over Ramirez et al. alone and in combination with other the other references listed in the previous Office Action.